

Klinično patološke značilnosti pacientk z rakom nožnice v obdobju med 1995 in 2017

Clinicopathological characteristics of patients with vaginal cancer in the period 1995 to 2017

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Izvleček

Namen: Rak nožnice je redek karcinom, ki predstavlja 3 % vseh malignomov ženskega reproduktivnega trakta z letno incidenco okoli 20 novih primerov na območju celotne Slovenije. Namen raziskave je bil oceniti značilnosti bolnic z rakom nožnice ter analizirati epidemiologijo, opisati klinične značilnosti, načine zdravljenja in dejavnike, ki vplivajo na pojavnost.

Metode: Retrospektivna raziskava je zajela bolnice z območja severovzhodne Slovenije, ki smo jih zaradi raka nožnice obravnavali med leti 1995 in 2017. Zabeležili smo njihove demografske značilnosti, značilnosti bolezni, klinične značilnosti, citološke in histološke izvide ter načine zdravljenja. Podatke smo statistično obdelali in ocenili povezavo med različnimi demografskimi značilnostmi, tumorskimi karakteristikami,

Abstract

Purpose: Vaginal cancer is a rare malignancy that is approximately 3% of all malignant neoplasms of the female genital tract and accounting for approximately 20 new diagnoses each year in Slovenia. The aim of this study was to evaluate characteristics of patients with vaginal cancer and to analyse the epidemiology and describe clinical features, types of treatments applied and factors affecting occurrence of the disease.

Methods: A retrospective study of all vaginal cancers in patients residing in northeastern Slovenia during the years 1995 and 2017 was performed. Patient demographics, disease characteristics, clinical features, referring cytology and histological findings and type of therapy were recorded. Associations among various demographic factors, tumour characteristics, treatments and

zdravljenjem in dejavniki tveganja.

Rezultati: Skupno smo v časovnem okvirju 23 let zbrali podatke 33 bolnic, ki so bile stare med 38 in 87 let. Povprečna starost bolnic je bila 64 let. Identificirali smo 5 različnih vrst neoplazij. Devetinšestdeset odstotkov obolelih bolnic je bilo starih med 50 in 80 let. Najpogosteje zabeležen histološki tip raka nožnice je bil ploščatocelični karcinom (78 %).

Zaključek: Ugotovili smo, da je ploščatocelični karcinom najpogostejša oblika raka nožnice v večjem delu slovenske populacije in pretežno prizadene starejše ženske. Izvedena raziskava je prvo poročilo na področju rakastih obolenj nožnice na slovenskem področju. Vključitev vseh bolnic z rakom nožnice iz drugih centrov v Sloveniji bi omogočila celovitejše in bolj reprezentativne zaključke.

risk factors of vaginal cancer were evaluated.

Results: A total of 33 patients aged 38–87 years were identified over the 23-year period. The mean age of patients was 64 years. Altogether, we found five different types of neoplasia and 97% of affected patients were between 50 and 80 years old. The most common histologic type of vaginal malignancy was squamous cell carcinoma (78%).

Conclusion: Our results suggested that in eastern Slovenian population, squamous cell carcinoma is the most common vaginal malignancy; it affected primarily older women. This research is first of its kind in the field of vaginal malignancies in the reported region. Retrieval of data from other medical centres of Slovenia would allow more valuable conclusions.

INTRODUCTION

Vaginal cancer is a rare gynecological malignancy that predominantly presents in women of older age. In Slovenia, the incidence of vaginal cancer is 1.1 per 100,000 women, with more than 50% over the age of 75 (1). The most common primary vaginal cancer type is squamous cell carcinoma (SCC), accounting for approximately 85% of diagnoses. Another common histological type is adenocarcinoma, which is about 10% of vaginal cancers (2,3). Also reported are cases of vaginal melanoma, leiomyosarcoma and endometrioid carcinoma (4,5).

Due to the rarity of vaginal cancer, its biological and risk factors are not as frequently studied as other female genital tract tumours. Therefore, the exact cause of vaginal cancer is still unclear (6). Several risk factors have been identified and depend on the histological type (2). SCC shares some risk factors with cervical carcinoma. The most important association is proposed to be between infection with the high-risk human papilloma virus (HPV-16) and vaginal cancer (6-8). The specific entity of vaginal intraepithelial neoplasia (VAIN), a precancerous stage that could be a precursor of vaginal cancer, is strongly connected with persistent HPV infection (8,9). Not all women who are infected with oncogenic HPV develop vaginal cancer, therefore additional factors such as history

of anogenital cancer (especially cervical cancer), cigarette smoking and decreased immune function could be considered important risk factors (6-9). Some adenocarcinomas are associated with in utero exposure to diethylstilbestrol (2,5,10). Reports indicate that a prior hysterectomy due to benign, premalignant, or malignant disease, could be responsible for vaginal cancer occurrence (10,11).

In spite of its low incidence, vaginal cancer is an important disease and its impact on women's health should not be underestimated. To our best knowledge, no single retrospective review has covered Slovenian patients with vaginal cancer. As the country's second largest tertiary centre, our patients receive primary surgical treatment at the Department for Gynecological Oncology and Oncology of the Breast and are referred to other tertiary facilities for radiotherapy and/or chemotherapy when required. The aim of this study was to review vaginal cancers recorded in Maribor's tertiary centre over the 23-year period 1995–2017 to document vaginal cancer status in the population of northeastern Slovenia.

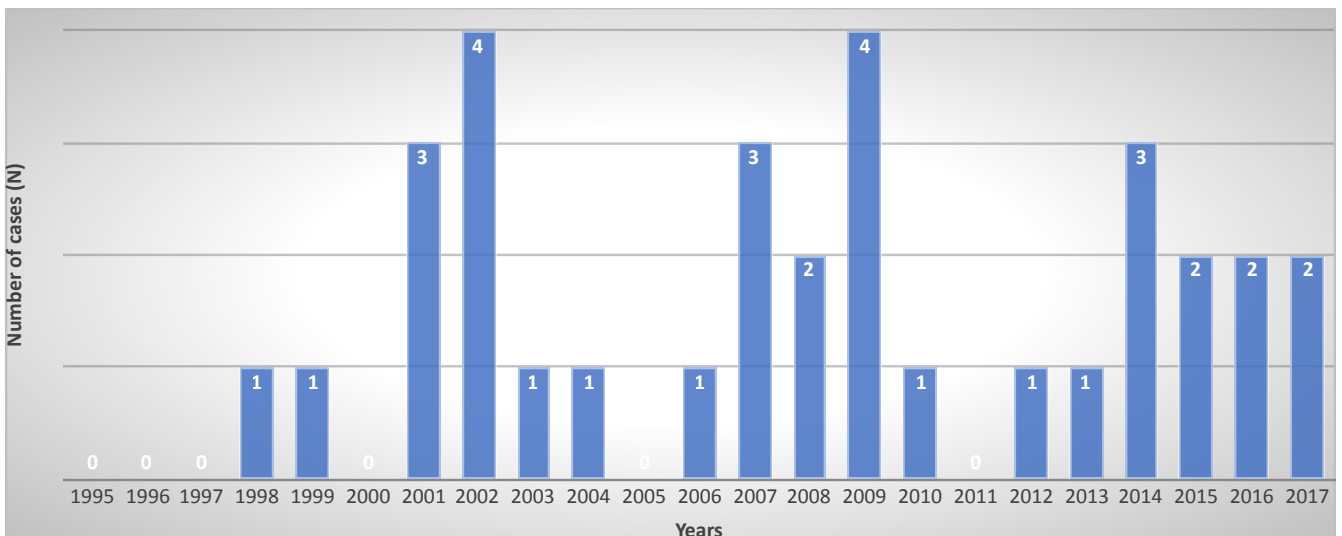
PATIENTS AND METHODS

A retrospective study was performed in which we collected clinical data on all vaginal tumours registered at the Clinical Department of Gynaecology and Perinatology of University Medical Centre Maribor from January 1995 to December 2017. This tertiary centre covers the northeastern part of Slovenia that has approximately 800,000 inhabitants. This study included all instances of vaginal cancer that were histologically confirmed by either biopsy or excised tissue. Demographic data, medical history and all cancer treatment data were collected in predefined written forms and digitalized using custom built Microsoft Access

databases. Study parameters included age, clinical presentation, and the presence of previous or coexisting genital disease, other malignant or premalignant gynecological disease, or other malignancies. Medical history, risk factors and lesion pathological type were recorded.

All patients diagnosed with cancer were staged according to the International Federation of Gynaecology and Obstetrics (FIGO) staging system from 2009. IBM SPSS Statistics Version 21 was used for statistical evaluation. Due to the retrospective nature of this study the approval of an ethics committee was not required.

Table 1: Yearly occurrence of vaginal cancer, 1995–2017



RESULTS

A total of 33 patients with vaginal cancer were identified in the records of the University Medical Centre Maribor between 1995 and 2017 (Table 1). Patients ranged in age from 38 to 87 years (median age 64 years) with most between 50 and 80 years of age (Table 2). Table 1 shows that the highest yearly occurrences for all vaginal cancers were in two peaks in years

Table 2: Age distribution of vaginal cancer

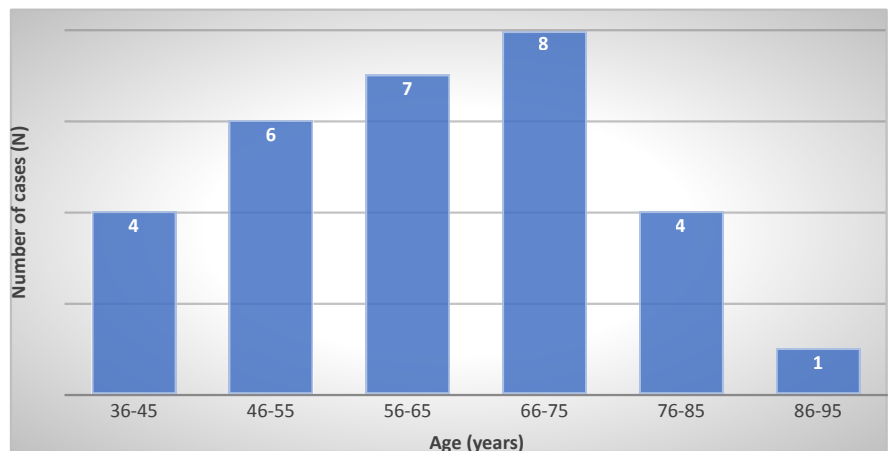
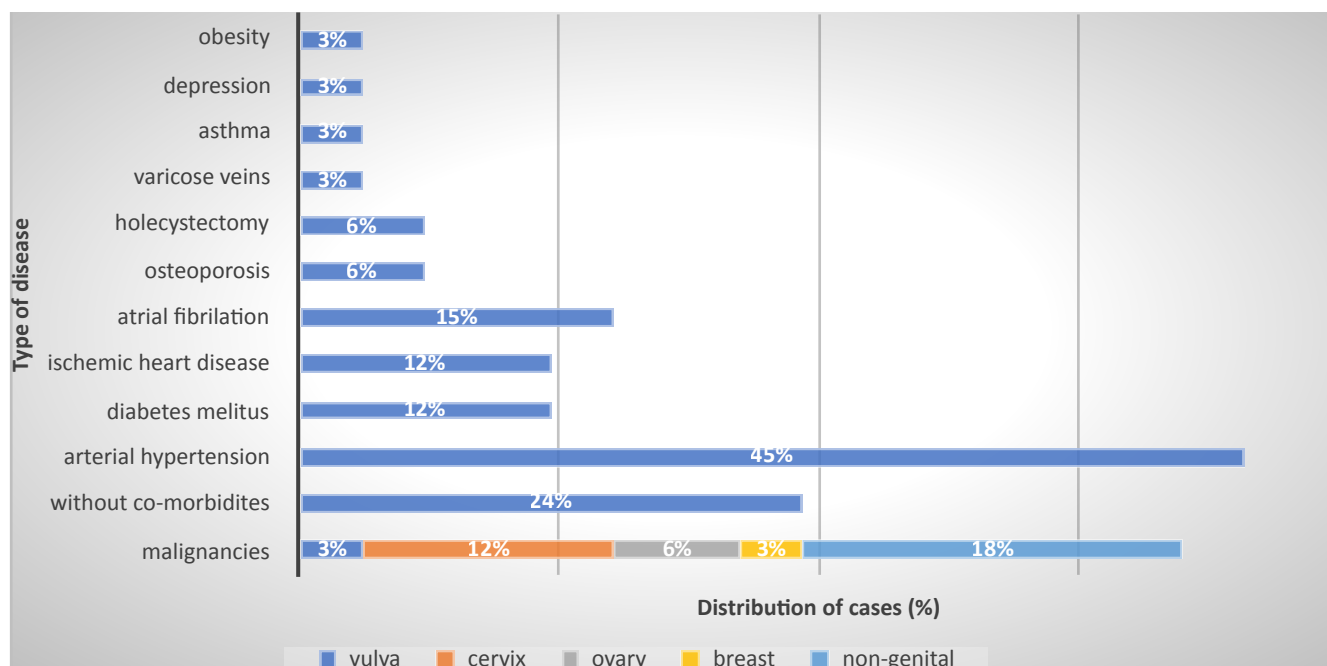


Table 3: History of other diseases or malignancies

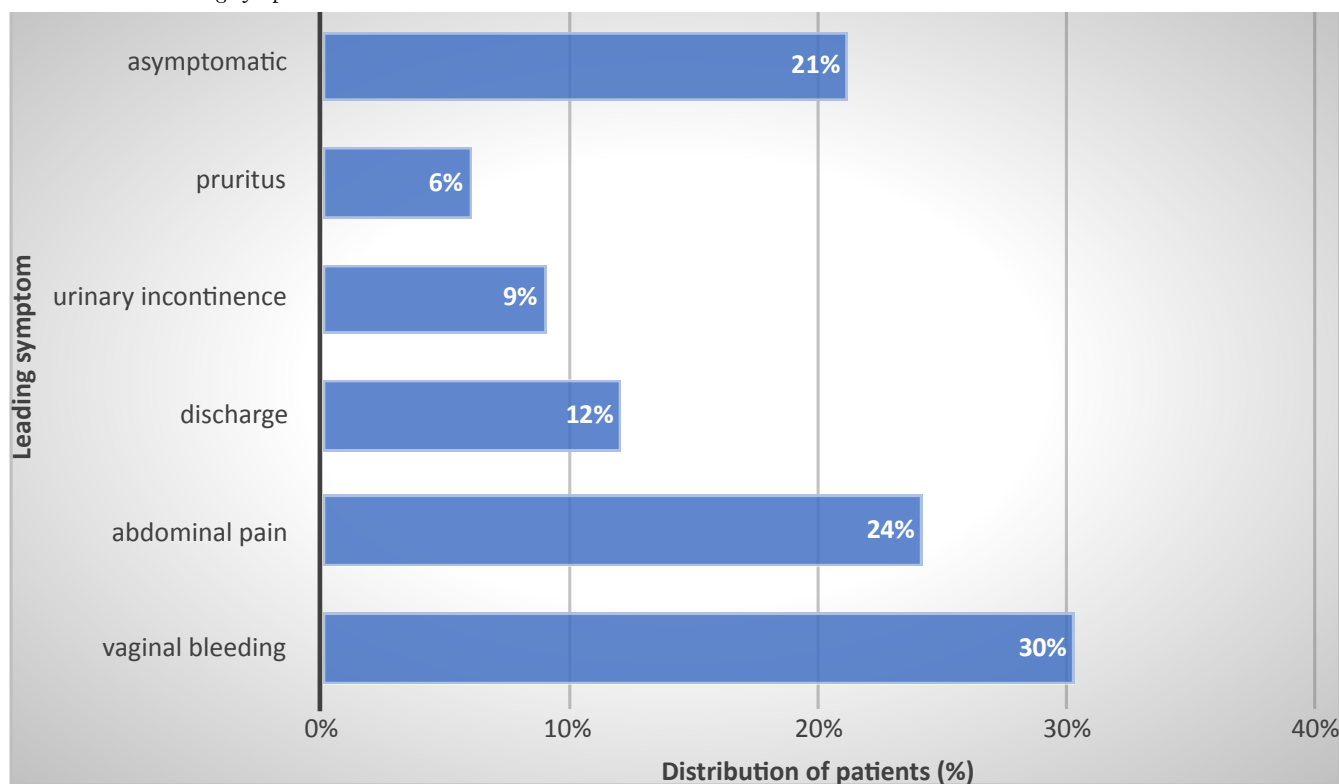


2002 and 2009. In most years, not more than three patients had vaginal cancers.

Comorbidities included hypertension in 15 (46%) patients, diabetes in four (12%), and atrial fibrillation in four (15%) (Table 3). A history of malignancy or

present malignancy was found for 14 women (42%) and 11 (29%) reported past or present premalignant lesions. Cervical intraepithelial neoplasia (CIN of unknown grade) was the most common histological finding, in eight (33%) patients. Information regarding

Table 4: Presenting symptoms



primary clinical presentation was available for 30 of the 33 patients: 10 (30%) had vaginal bleeding, eight had (24%) abdominal pain and seven (21%) patients were asymptomatic (Table 4).

The most frequently diagnosed histological type of vaginal tumor was SCC (78%), followed by adenocarcinoma (9%), vaginal sarcoma (4%), and diffuse non-Hodgkin lymphoma (4%) with one vaginal cancer

lacking information about histological subtype (Table 5). Precancerous lesions were diagnosed in 10 women and subsequently divided into VAIN 1 (10%), VAIN 2 (20%), VAIN 3 (60%) and VIN 3 (10%) (Table 5a). According to FIGO classification, 21% of patients had vaginal cancer that was stage I, 52% had cancer that was stage II, 4% had stage III and 21% had stage IV disease.

Table 5: Histological types of vaginal cancer, 1995–2017

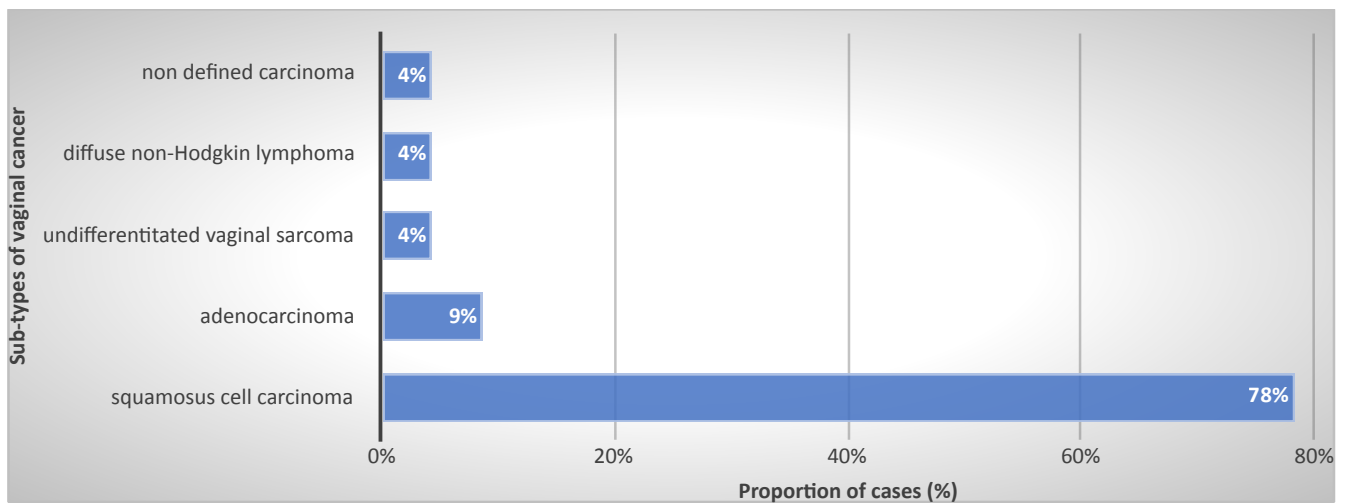
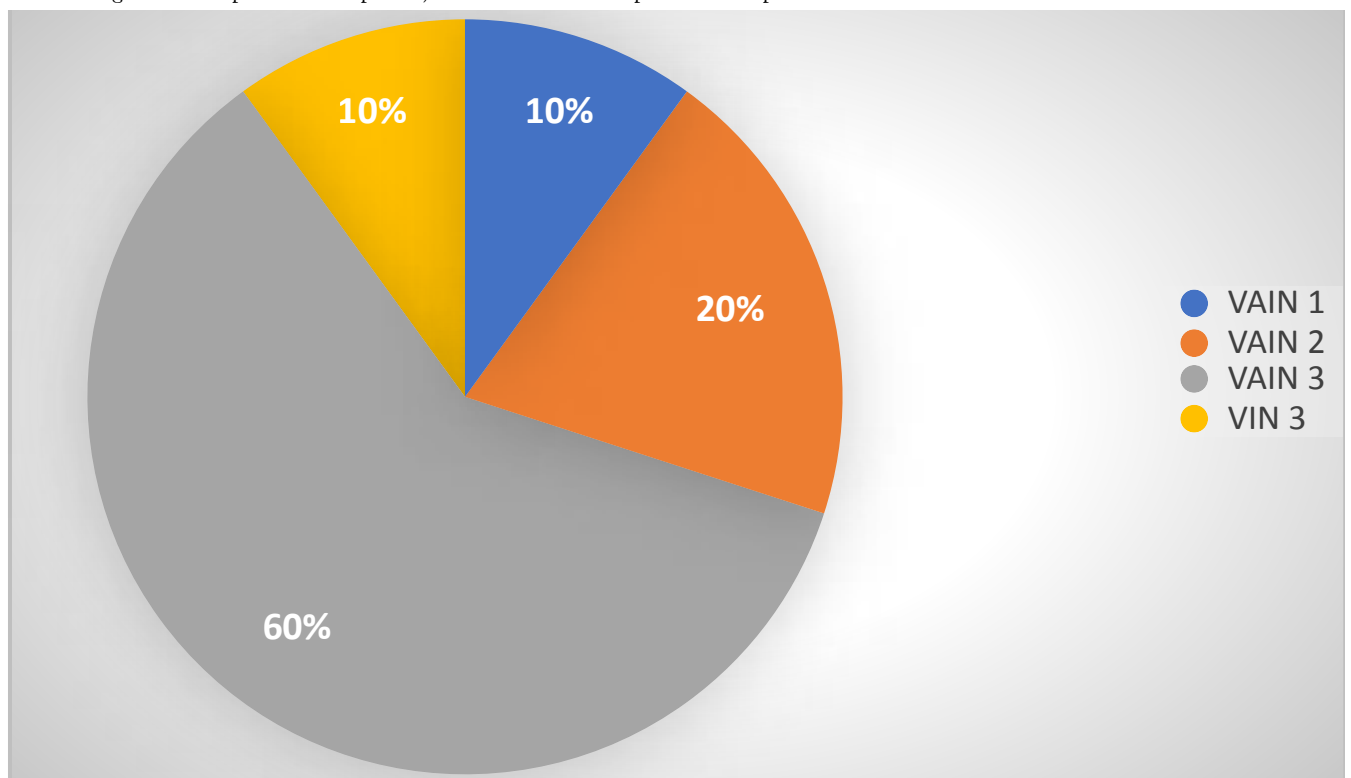


Table 5a: Histological sub-types of precancerous lesions, 1995-2017

VAIN=vaginal intraepithelial neoplasia; VIN=vulvar intraepithelial neoplasia



Primary radiotherapy was the most common primary treatment modality, applied in 35% of patients. In 21% of patients, the initial treatment was surgical, with procedures including wide local excision. In 8% of patients with surgery, those procedures were followed by adjuvant radiotherapy with 2 (8%) of patients receiving a combination of chemotherapy and radiotherapy. Palliative radiotherapy or other symptomatic treatment was offered to 21% of patients with advanced disease.

DISCUSSION

This study was primarily conducted to gather information about patients with any kind of malignant pathology of the vagina. Until now, little or no medical information in the field of vaginal malignancies has been available for patients in our region.

Slovenia has a population of approximately 2.1 million people and the tertiary activities of University Medical Centre Maribor covers about 800,000 patients from the northeastern part of the country. Of this region, 19.1% of the population is above the age of 65 with a slight female predominance (51.4%) and a large majority of inhabitants who are Caucasian (12).

Our results showed squamous cell carcinoma was the most common histological type of vaginal cancer identified (78%), followed by adenocarcinoma (9%). This result was similar to reports from other countries indicating squamous cell carcinoma as the most common type of vaginal malignancy (13). Undifferentiated vaginal sarcoma, diffuse non-Hodgkin lymphoma, metastasis from ovarian adenocarcinoma and undefined carcinoma were each found in a single patient (4.2% each) and altogether accounted for 12% of all vaginal cancers. Precancerous lesions such as VAIN 1-3 and VIN 3 tumours were observed with a distribution of VAIN 1, 10%; VAIN 2, 20%; VAIN 3, 60%; and VIN 3, 10%. This high distribution of precancerous lesions could be a consequence of early recognition and diagnosis of vaginal disease and could also represent patient awareness about the importance of regular gynecological examinations. Although the group with VAIN 1-3 disease was large,

only one patient with VAIN 1 disease was recorded. The age distribution of patients with vaginal cancer in this study (69% between 50 and 80 years) is similar to international reports (13). The median age of patients was 64 years, which also explained the prevalence of comorbidities recorded in our patient group. A study by Siegler et al. suggests that almost half of vaginal cancers are associated with metastases from other organs and almost half of VAIN 3 cancers are associated with past cervical dysplasia or carcinoma (13). In our database, however, only one patient had metastasis from ovarian cancer and that patient was excluded from analyses.

International data report several risk factors that contribute to the development of vaginal neoplasia, with high risk HPV infection as the major factor (14). Lack of HPV sample data prevented us from gathering enough relevant or reliable information on this factor. Advanced age, five or more lifetime sexual partners, and current smoker status at diagnosis are other risk factors that are also common in cervical cancer (10). Furthermore, prior hysterectomy or previously treated anogenital tumours are proposed as risk factors (10). We were limited in our personal data and past medical histories of our patients. These records were often lacking detailed information, so we cannot make specific conclusions regarding risk factors such as smoking or number of sexual partners. However, we found that four (12%) of our patients had a past hysterectomy. Several retrospective cohort studies concluded that patients with CIN 3 disease have a significantly increased rate of developing vaginal cancer compared with all women in the same population and time period (15-18). This finding was confirmed in our study, since CIN of undetermined stage was present in 18% of patients.

The primary clinical presentations in our study were 30% of patients complaining of vaginal bleeding and 12% having discharge. Therefore, we came to the same conclusion as other studies in finding them as the most common symptoms (2,5). Furthermore, our study found that 21% of patients reported no symptoms, also comparable with international data (3). Extending the study and obtaining more information about patient treatments would be interesting, but most patients were referred to the Institute of Oncol-

ogy in Ljubljana and we did not have the opportunity to obtain those medical files. The standard internationally accepted treatment is radiotherapy with external beam radiation and/or brachytherapy, depending on the extent, thickness, location and morphology of the lesion. Only 35% of patients receive radiotherapy as primary treatment, however (11,19,20). The role of chemotherapy in treatment of vaginal neoplasia has not been fully evaluated and two (9%) patients in this study were treated with some form of chemotherapy (11).

Because the incidence of vaginal carcinoma is low, we expanded our time frame to obtain as many patients as possible and gather information about the basic clinicopathological characteristics of patients with vaginal cancer. Our study had several limitations. One challenge was that the information was scattered in the medical archives of individual patients and the study was retrospective. The scale of the samples might be problematic and we cannot generalize information to the entire population. However, this study gathered

basic clinicopathological characteristics of the patients with vaginal carcinoma and could be used as a platform for more detailed studies on causality and treatment.

CONCLUSION

In conclusion, this study found that in eastern Slovenian population, squamous cell carcinoma was the most common vaginal malignancy and affected primarily older women. However, due to its retrospective nature, this study had potential limitations, because the data collected were limited to reports in medical charts. Additionally, vaginal cancer is a rare cancer and although observed time span was 23 years, the number of diagnoses was as low as expected. To overcome this limitation, data from other medical centres should be included to create larger, more representative samples. Moreover, we encourage the prospective collection of as much clinical data as possible in a clinical registry supported by modern information technology.

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